SN 09/582,524
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This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

151-153 (canceled)

154. (currently amended) The method according to claim ~~151~~ 211, wherein said labeling means comprises labeled antigen.

155. (currently amended) The method according to claim ~~151~~ 211, wherein said labeling means comprises a non-immobilized labeled antibody, wherein said non-immobilized labeled antibody binds with said antigen at a binding site distinct from a binding site for either (i) said autoantibody or autoantibodies being screened for or (ii) said immobilized antibody or antibodies, whereby in step (d), antigen is allowed to be bound both to said immobilized ~~antibody~~ antibodies and to said non-immobilized antibody.

156. (currently amended) The method according to claim ~~151~~211, further comprising providing a ~~positive~~ control which provides a positive signal ~~that is present~~ in the presence or absence of the autoantibody or autoantibodies being screened.

157. (previously added) The method according to claim 156, wherein the positive control comprises at least one control antibody to the antigen, said control antibody attached to the substrate, wherein said control antibody binds to a site on the antigen distinct from a binding site thereof for the autoantibody or autoantibodies being screened.

158. (currently amended) The method according to claim ~~151~~211, wherein said antigen is a thyroid protein.

159. (currently amended) The method according to claim ~~151~~211, wherein said antigen is thyroid stimulating hormone receptor.

160. (currently amended) The method according to claim ~~151~~211, wherein said antigen is selected from the group consisting of thyroid peroxidase and thyroglobulin.

161. (currently amended) The method according to claim ~~151~~211, further comprising screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.

162. (currently amended) The method according to claim ~~151~~211, wherein said monitoring comprises observing a colorimetric change dependent on said binding of said autoantibody or autoantibodies with said antigen.

163. (currently amended) The method according to claim ~~151~~211, wherein said labeling means is colloidal gold.

164. (currently amended) The method according to claim ~~151~~211, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.

165. (currently amended) The method according to claim ~~151~~211, wherein said substrate comprises an application zone provided upstream of said immobilized ~~antibody~~ antibodies on said substrate, and wherein said mixture is allowed to flow from said application zone along said substrate to said immobilized ~~antibody~~ antibodies.

166. (previously added) The method according to claim 165, wherein said application zone contains said source of said antigen, and said mixture is obtained by contacting said sample of body fluid with said antigen in said application zone.

167. (previously added) The method according to claim 166, wherein said substrate further comprises at least one non-immobilized antibody to said antigen , wherein said non-immobilized antibody is provided downstream of said antigen source in said application zone.

168. (currently amended) A method of screening a sample of body fluid for first and / or second autoantibodies to at least one antigen, which method comprises:

(a) providing a first antibody to said antigen, wherein said first antibody is immobilized on a substrate;

(b) providing a second antibody to said antigen, wherein said second antibody is labeled to permit monitoring of binding of said autoantibodies and said antigen, and is non-immobilized so that said second antibody can flow along said substrate;

(c) providing a source of said at least one antigen, said antigen comprising a first binding site to which either the first autoantibody or the immobilized antibody binds and a second binding site to which either the second autoantibody or the non-immobilized antibody binds;

(d) contacting ~~(i)~~ said antigen ~~source~~ of step (c), ~~(ii)~~ said sample of body fluid and simultaneously or successively ~~(iii)~~ said non-immobilized antibody, so as to obtain a mixture wherein said antigen binds with autoantibodies present in said sample of body fluid and / or said non-immobilized antibody;

(e) allowing said mixture obtained in step (d) to flow along said substrate of step (a) to said immobilized antibody;

(f) ~~providing labeling means so as to permit monitoring of binding of said autoantibodies and said antigen; and~~

~~(g)~~ monitoring said binding so as to provide an indication of the presence of said autoantibodies in said sample of body fluid;

~~whereby~~ wherein said first and / or second autoantibodies, when present in said sample being screened, bind with said first and / or second binding sites of said antigen in step (d) respectively so that subsequent binding of said immobilized and / or non-immobilized antibodies with said first and / or second binding sites of said antigen respectively is ~~precluded~~ inhibited where the first and / or second autoantibodies have previously bound with said first and / or second binding sites of said antigen in step (d).

169. (canceled)

170. (currently amended) The method according to claim 168, further comprising providing a ~~positive~~ control ~~that is present~~ which provides a positive signal in the presence or absence of the autoantibody or autoantibodies being screened.

171. (previously added) The method according to claim 170, wherein said positive control comprises attaching to the substrate at least one control agent that binds to the at least one non-immobilized antibody.

172. (previously added) The method according to claim 168, wherein said antigen is a thyroid protein.

173. (previously added) The method according to claim 168, wherein said antigen is thyroid stimulating hormone receptor.

174. (previously added) The method according to claim 168, wherein said antigen is selected from the group consisting of thyroid peroxidase and thyroglobulin.

175. (previously added) The method according to claim 168, further comprising screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.

176. (previously added) The method according to claim 168, wherein said monitoring comprises observing a colorimetric change dependent on said binding of said autoantibody or autoantibodies with said antigen.

177. (previously added) The method according to claim 168, wherein said labeling means is colloidal gold.

178. (previously added) The method according to claim 168, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.

179. (previously added) The method according to claim 168, wherein said substrate comprises an application zone provided upstream of said immobilized antibody on said substrate, and wherein said mixture is allowed to flow from said application zone along said substrate to said immobilized antibody.

180. (previously added) The method according to claim 179, wherein said application zone contains said source of said antigen, and said mixture is obtained by contacting said sample of body fluid with said antigen in said application zone.

181. (previously added) The method according to claim 180, wherein said substrate further comprises the non-immobilized second antibody to said antigen, wherein said non-immobilized second antibody is provided downstream of said antigen source in said application zone.

182-183 (canceled)

184. (currently amended) A kit ~~The kit according to claim 183~~ for screening a sample of body fluid for at least first and second autoantibodies to at least one antigen, wherein said kit ~~antigen~~ comprises:

(a) at least first and second antibodies to said antigen immobilized on a substrate;

(b) a source of said at least one antigen, the antigen having

a first binding site to which either said first autoantibody or said first immobilized antibody binds, whereby subsequent binding of said first immobilized antibody with said first binding site is precluded where said first autoantibody has previously bound with said first binding site; and

a second binding site to which either said second autoantibody or said second immobilized antibody binds, whereby subsequent binding of said second immobilized antibody with said second binding site is precluded where said second autoantibody has previously bound to said second binding site;

wherein said first and second binding sites are distinct sites on said antigen;

(c) means for contacting said antigen source with said sample of body fluid, so as to obtain a mixture wherein said antigen binds with autoantibodies present in said sample of body fluid;

(d) means for allowing said mixture to flow along said substrate to said antibodies immobilized to said substrate; and

(e) labeling means so as to permit monitoring of binding of said autoantibodies and said antigen, so as to provide an indication of the presence of said autoantibodies in said sample of body fluid.

185. (currently amended) The kit according to claim ~~182~~184, wherein said labeling means comprises labeled antigen.

186. (currently amended) The kit according to claim ~~182~~184, wherein said labeling means comprises a non-immobilized labeled antibody, which non-immobilized labeled antibody binds with a site on said antigen distinct from a binding site for

either (i) said ~~autoantibody or~~ autoantibodies being screened or (ii) said immobilized ~~antibody or~~ antibodies, whereby antigen is allowed to be bound both to said immobilized ~~antibody~~ antibodies and to said non-immobilized labeled antibody.

187. (currently amended) The kit according to claim ~~182~~184, further comprising a ~~positive~~ control ~~that is present~~ which provides a positive signal in the presence or absence of the ~~autoantibody or~~ autoantibodies being screened.

188. (currently amended) The kit according to claim 187, wherein the ~~positive~~ control comprises at least one control antibody to the antigen attached to the substrate, wherein the control antibody binds to a site on the antigen distinct from a binding site thereof for the ~~autoantibody or~~ autoantibodies being screened.

189. (currently amended) The kit according to claim ~~182~~184, wherein said antigen is a thyroid protein.

190. (currently amended) The kit according to claim ~~182~~184, wherein said antigen is thyroid stimulating hormone receptor.

191. (currently amended) The kit according to claim ~~182~~184, wherein said antigen is selected from the group consisting of thyroid peroxidase and thyroglobulin.

192. (currently amended) The kit according to claim ~~182~~184, further comprising means for screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.

193. (currently amended) The kit according to claim ~~182~~184, wherein said labeling means is colloidal gold.

194. (currently amended) The kit according to claim ~~182~~184, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.

195. (currently amended) The kit according to claim ~~182~~184, wherein said substrate comprises an application zone provided upstream of said immobilized ~~antibody~~ antibodies on said substrate.

196. (previously added) The kit according to claim 195, wherein said application zone contains said source of said antigen.

197. (previously added) The kit according to claim 196, wherein said substrate further comprises at least one non-immobilized antibody to said antigen, wherein said non-immobilized antibody is provided downstream of said antigen source in said application zone.

198. (currently amended) A kit for screening a sample of body fluid for first and / or second autoantibodies to at least one antigen, which ~~method~~ kit comprises:

(a) a first antibody to said antigen, wherein said first antibody is immobilized on a substrate;

(b) a second antibody to said antigen, wherein said second antibody is labeled to permit monitoring of binding of said autoantibodies and said antigen, and is non-immobilized so that said second antibody can flow along said substrate when present in a mixture;

(a) a source of said at least one antigen, said antigen comprising a first binding site to which either the first autoantibody or the immobilized antibody binds and a second binding site to which either the second autoantibody or the non-immobilized antibody binds;

(d) means for contacting (i) said antigen source, (ii) said sample of body fluid and simultaneously or successively (iii) said non-immobilized second antibody, so

as to obtain a mixture wherein said antigen binds with autoantibodies present in said sample of body fluid and / or said non-immobilized antibody; and

(e) means for allowing said mixture to flow along said substrate to said immobilized antibody;

~~(f) labeling means so as to permit monitoring of binding of said autoantibodies and said antigen, so as to provide an indication of the presence of said autoantibodies in said sample of body fluid~~.

199. (canceled)

200. (previously added) The kit according to claim 198, further comprising a ~~positive~~ control ~~that is present~~ which provides a positive signal in the presence or absence of the autoantibody or autoantibodies being screened.

201. (previously added) The kit according to claim 200, wherein the positive control comprises at least one control agent attached to the substrate and binds to the at least one non-immobilized antibody.

202. (previously added) The kit according to claim 198, wherein said antigen is a thyroid protein.

203. (previously added) The kit according to claim 198, wherein said antigen is thyroid stimulating hormone receptor.

204. (previously added) The kit according to claim 198, wherein said antigen is selected from the group consisting of thyroid peroxidase and thyroglobulin.

205. (previously added) The kit according to claim 198, further comprising means for screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.

206. (previously added) The kit according to claim 198, wherein said labeling means is colloidal gold.

207. (previously added) The kit according to claim 198, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.

208. (previously added) The kit according to claim 198, wherein said substrate comprises an application zone provided upstream of said immobilized antibody on said substrate.

209. (previously added) The kit according to claim 208, wherein said application zone comprises said source of said antigen.

210. (previously added) The kit according to claim 209, wherein said substrate further comprises the non-immobilized second antibody to said antigen, wherein said non-immobilized second antibody is provided downstream of said antigen source in said application zone.

211. (new) A method of screening a sample of body fluid for at least first and/or second autoantibodies to at least one antigen, which method comprises:

(a) providing at least first and/or second antibodies to said antigen, wherein said first and/or second antibodies are immobilized on a substrate and bind first and second distinct binding sites, respectively, on said antigen;

(b) providing a source of said at least one antigen, wherein said antigen comprises at least first and second distinct binding sites, wherein said first binding site binds said first autoantibody or said first immobilized antibody, and said second binding site binds said second autoantibody or said second immobilized antibody;

(c) contacting said antigen of step (b) with said sample of body fluid, so as to obtain a mixture wherein said antigen binds with autoantibodies present in said sample of body fluid;

(d) allowing said mixture obtained in step (c) to flow along said substrate of step (a) to said first and/or second antibodies immobilized on said substrate;

(e) providing labeling means so as to permit monitoring of binding of said autoantibodies and said antigen; and

(f) monitoring said binding so as to provide an indication of the presence of said autoantibodies in said sample of body fluid;

wherein said first and second autoantibodies, when present in said sample being screened bind with said antigen in step (c) so that in step (d) binding of said first and/or second immobilized antibodies to said first and second binding sites on said antigen is inhibited where the first and second autoantibodies have bound with the first and second binding sites of said antigen in step (c).

212. (new) A method of screening a sample of body fluid for at least first and/or second autoantibodies respectively binding at least first and second distinct antigens, which method comprises:

(a) providing at least first and/or second antibodies to said at least first and second distinct antigens, wherein said first and/or second antibodies are immobilized on a substrate;

(b) providing one or more sources of said at least first and second distinct antigens;

(c) contacting said at least first and second antigens of step (b) with said sample of body fluid, so as to obtain a mixture wherein said first and second antigens respectively bind with said first and/or second autoantibodies when present in said sample of body fluid;

(d) allowing said mixture obtained in step (c) to flow along said substrate of step (a) to said first and/or second antibodies immobilized to said substrate;

(e) providing labeling means so as to permit monitoring of said binding of said autoantibodies and said antigens; and

(f) monitoring said binding so as to provide an indication of the presence of said autoantibodies in said sample of body fluid;

wherein said first and second autoantibodies when present in said sample being screened bind with said first and second antigens in step (c) respectively so that in step (d) binding of said first and second immobilized antibodies with said first and second antigens respectively is inhibited where the first and second antoantibodies have bound with the first and second antigens in step (c).

213. (new) A method of screening a sample of blood for at least one autoantibody to at least one antigen, which method comprises:

(a) providing a test strip which includes a sample application zone for receiving said blood sample being screened and which sample application zone includes means for separating blood cells from plasma;

(b) providing at least one antibody to said antigen, which antibody is immobilized on said test strip downstream of said sample application zone;

(c) providing a source of said at least one antigen, wherein said antigen has at least one binding site that can be bound by either said autoantibody or said immobilized antibody;

(d) contacting said antigen of step (c) with either said blood sample, or separated plasma obtained therefrom, prior to, simultaneously with, or subsequent to, application of said blood sample to said application zone of said test strip whereby blood cells are separated from said plasma, so as to obtain a mixture wherein said at least one autoantibody being screened binds said at least one binding site of said at least one antigen;

(e) allowing said mixture obtained in step (d) to flow along said test strip to said at least one antibody of step (b) immobilized on said test strip;

(f) providing labeling means so as to permit monitoring of said binding of said at least one autoantibody and said antigen; and

(g) monitoring said binding so as to provide an indication of the presence of said at least one autoantibody in said blood sample;

wherein when said at least one autoantibody being screened is present in said sample, said autoantibody binds with said at least one binding site of said antigen in step (d), and inhibits subsequent binding of said immobilized antibody to said at least one binding site of said antigen in step (e).

214. (new) A method of screening a sample of body fluid for at least one autoantibody to at least one antigen, which method comprises:

(a) providing at least one antibody immobilized on a substrate and which immobilized antibody binds a common binding site of said antigen to which said at least one autoantibody being screened also binds;

(b) providing a source of said at least one antigen, wherein said antigen includes said common binding site and is labeled to permit monitoring of binding of said antigen with said at least one autoantibody;

(c) contacting said antigen of step (b) with said sample of body fluid, so as to obtain a mixture wherein said at least one antigen binds with said at least one autoantibody being screened when present in said sample of body fluid;

(d) allowing said mixture obtained in step (c) to flow along said substrate of step (a) to said at least one antibody immobilized to said substrate; and

(e) monitoring said binding so as to provide an indication of the presence of said at least one autoantibody in said sample of body fluid;

wherein said at least one autoantibody when present in said sample being screened binds with said common binding site of said at least one antigen in step (c) so that in step (d) binding of said at least one immobilized antibody with said common binding site of said at least one antigen is inhibited where said at least one antoantibody has bound with the common binding site of said antigen in step (c).